

§Appl. No. 09/869,709
Amdt. dated October 5, 2004
Supplemental Reply to Office Action of, April 5, 2004

Listing of Claims:

Please **amend** the claims as follows:

Claim 1 (Currently Amended) A transformed cell comprising, a human epidermal growth factor type membrane receptor and a fusion protein comprising an effector polypeptide which is a constitutively active human ras polypeptide fused to an adaptor polypeptide which is Grb2 polypeptide, wherein upon binding of ligand to said receptor, said fusion protein binds to said receptor via said adaptor polypeptide.

Claim 2 (Cancel)
Claim 3 (Cancel)
Claim 4 (Cancel)
Claim 5 (Cancel)
Claim 6 (Cancel)
Claim 7 (Cancel)
Claim 8 (Cancel)
Claim 9 (Cancel)
Claim 10 (Cancel)
Claim 11 (Cancel)
Claim 12 (Cancel)
Claim 13 (Cancel)
Claim 14 (Cancel)
Claim 15 (Cancel)
Claim 16 (Cancel)
Claim 17 (Cancel)

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Claim 18 (Cancel)

Claim 19 (Cancel)

Claim 20 (Cancel)

Claim 21 (Cancel)

Claim 22 (Cancel)

Claim 23 (Cancel)

Claim 24 (Previously Presented) A cell as claimed in claim 1, wherein the receptor is a tyrosine kinase.

Claim 25 (Cancel)

Claim 26 (Previously Presented) A cell as claimed in claim 1, wherein the cell is a prokaryotic or eukaryotic cell.

Claim 27 (Previously Presented) A cell as claimed in claim 1, wherein the cell is a yeast cell.

Claim 28 (Previously Presented) A cell as claimed in claim 1, wherein said cell is immobilized on a solid carrier.

Claim 29 (Previously Presented) A cell as claimed in claim 28, wherein the cell is immobilized on biochips or enclosed in microchambers.

Claim 30 (Currently Amended) A cell as claimed in claim 1, wherein in the absence of the membrane receptor a Ras or Ras-like signal pathway in the cell cannot be activated.

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Claim 31 (Currently Amended) A cell as claimed in claim 30, wherein the activatability of the Ras ~~or Ras-like~~ signal pathway is temperature-dependent in the absence of the membrane receptor.

Claim 32 (Currently Amended) A cell as claimed in claim 31, wherein the lack of activatability of the Ras ~~or Ras-like~~ signal pathway in the absence of the membrane receptor above a particular temperature is derived from at least one mutation of a guanine nucleotide exchange factor intrinsic to the cell, which has the effect that the latter is incapable of functioning above the particular temperature.

Claim 33 (Previously Presented) A cell as claimed in claim 32, wherein the cells are cells of the *Saccharomyces cerevisiae* yeast strain cdc25-2 or are derived therefrom.

Claim 34 (Currently Amended) A cell as claimed in claim 31, wherein the lack of activatability of the Ras ~~or Ras-like~~ signal pathway in the absence of the membrane receptor above a particular temperature is derived from at least one mutation of a Ras protein intrinsic to the cell, which has the effect that the latter is incapable of functioning above the particular temperature.

Claim 35 (Currently Amended) An *in vivo* assay for determining the suitability of a test substance as ligand for a ligand-binding section of a receptor, characterized by the following steps:

(a) contacting the test substance with cells as claimed in claim 30 under conditions with which a Ras ~~or Ras-like~~ signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains a ligand-binding section, and the fusion protein whose binding to the membrane receptor depends on the binding of a ligand to the

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ligand-binding section of the membrane receptor is able to activate this Ras ~~or Ras-like~~ signal pathway,

(b) investigating whether activation of the Ras ~~or Ras-like~~ signal pathway has taken place, where detection of the activation of the Ras ~~or Ras-like~~ signal pathway indicates the ability of the test substance to bind to the ligand-binding section.

Claim 36 (Currently Amended) An assay as claimed in claim 35, where step (b) comprises detecting the activation of the Ras ~~or Ras-like~~ signal pathway via reporter gene expression which takes place where appropriate and only because of the activation, resulting from the activation of the Ras ~~or Ras-like~~ signal pathway, of a specific transcription factor, where detection of the expression of the reporter gene indicates the ability of the test substance to bind to the ligand-binding section.

Claim 37 (Previously Presented) An assay as claimed in claim 35, where in step (a) cells in which the inactive or inactivatable Ras or Ras-like signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for cell reproduction are employed, and step (b) comprises investigating whether the cells are capable of reproduction under said conditions, where detection of the ability of the cells to reproduce indicates the ability of the test substance to bind to the ligand-binding section.

Claim 38 (Previously Presented) A *in vivo* assay for determining the suitability of a test substance as ligand for a ligand-binding section of a receptor, characterized by the following steps:

(a) contacting the test substance with cells as claimed in claim 30 under conditions with which a Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains said ligand-binding section, and the

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effector protein or polypeptide whose binding to a membrane component depends on the lack of binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 30, is able to activate this Ras or Ras-like signal pathway,

(b) investigating whether activation of the Ras or Ras-like signal pathway has taken place,

(c) investigating cells employed in step (a) under conditions with which the Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, for activation of the Ras or Ras-like signal pathway in the absence of the test substance, where detection of the activation of the Ras or Ras-like signal pathway in the absence of the test substance and the inactivity of the Ras or Ras-like signal pathway in the presence of the test substance indicates the ability of the test substance to bind to the ligand-binding section.

Claim 39 (Currently Amended) An assay as claimed in claim 35, ~~characterized in that wherein~~ the test substance is a naturally occurring substance ~~and, in particular,~~ an odorant, flavoring, peptide, peptide hormone, protein, ~~in particular~~ cytokine, growth factor, neurotransmitter, non-protein- or -peptide-like hormone and/or a vitamin.

Claim 40 (Currently Amended) An assay as claimed in claim 35, ~~characterized in that wherein~~ the test substance is a non-naturally occurring substance ~~and, in particular,~~ a synthetic derivative of a natural ligand, ~~or a poison, in particular~~ or dioxin.

Claim 41 (Currently Amended) An assay as claimed in claim 40, wherein the test substance is ~~employed as~~ a fusion protein comprising a ligand domain capable of binding to said membrane receptor.

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Claim 42 (Previously Presented) A screening method for unknown ligands of a particular receptor, characterized in that an assay method as claimed in claim 35 is employed for the screening.

Claim 43 (Currently Amended) An *in vivo* assay for determining the presence of a ligand for a ligand-binding section of a receptor in a sample which possibly contains the latter, characterized by the following steps:

(a) contacting the sample with cells as claimed in claim 30 under conditions with which a Ras or ~~Ras-like~~ signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains a ligand-binding section, and the fusion protein whose binding to the membrane receptor depends on the binding of a ligand to the ligand-binding section of the membrane receptor, is able to activate this Ras or ~~Ras-like~~ signal pathway,

(b) investigating whether activation of the Ras or ~~Ras-like~~ signal pathway has taken place, where detection of the activation of the Ras or ~~Ras-like~~ signal pathway indicates the presence of a ligand for the ligand-binding section of a receptor in the sample.

Claim 44 (Currently Amended) An assay as claimed in claim 43, where step (b) comprises detecting the activation of the Ras or ~~Ras-like~~ signal pathway via reporter gene expression which takes place where appropriate and only because of the activation, resulting from the activation of the Ras or ~~Ras-like~~ signal pathway, of a specific transcription factor, where detection of the expression of the reporter gene indicates the presence of a ligand for the ligand-binding section of a receptor in the sample.

Claim 45 (Original) An assay as claimed in claim 43, where in step (a) cells in which the inactive or inactivatable Ras or Ras-like signal pathway is a signal pathway which acts on the cell

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cycle and whose activation is essential for cell reproduction are employed, and step (b) comprises investigating whether the cells are capable of reproduction under said conditions, where detection of the ability of the cells to reproduce indicates the presence of a ligand for the ligand-binding section of a receptor in the sample.

Claim 46 (Previously Presented) An *in vivo* assay for determining the presence of a ligand for a ligand-binding section of a receptor in a sample which possibly contains the latter, characterized by the following steps:

(a) contacting the sample with cells as claimed in claim 30 under conditions with which a Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains a ligand-binding section, and the fusion protein whose binding to the membrane receptor depends on the lack of binding of a ligand to the ligand-binding section of the membrane receptor is able to activate this Ras or Ras-like signal pathway,

(b) investigating whether activation of the Ras or Ras-like signal pathway has taken place,

(c) investigating cells employed in step (a) under conditions with which the Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, for activation of the Ras or Ras-like signal pathway in the absence of the sample, where detection of the activation of the Ras or Ras-like signal pathway in the absence of the sample and the inactivity of the Ras or Ras-like signal pathway in the presence of the sample indicates the presence of a ligand for the ligand-binding section of a receptor in the sample.

Claim 47 (Previously Presented) A screening method for unknown ligands of a particular receptor in a sample, characterized in that an assay method as claimed in claim 43 is employed for the screening.

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Claim 48 (Previously Presented) An *in vivo* assay for the quantitative determination of the concentration of a ligand for a ligand-binding section of a receptor in a sample which contains the latter, characterized by the following steps:

(a) contacting an aliquot of the sample with cells as claimed in claim 30 under conditions with which a Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, where the membrane receptor contains said ligand-binding section, and the effector protein or polypeptide whose binding to a membrane component depends on the binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 30, is able to activate this Ras or Ras-like signal pathway,

(b) detecting quantitatively the extent of the activation of the Ras or Ras-like signal pathway by direct or indirect means,

(c) measuring the concentration of the ligand in the sample by comparing the measured extent of activation with corresponding values measured for known standard concentrations of the ligand.

Claim 49 (Previously Presented) An assay as claimed in claim 48, characterized in that the quantitative detection of the extent of activation of the Ras or Ras-like signal pathway in step (b) takes place indirectly by determining the amount present in the cells of a transcription or translation product of a reporter gene whose expression takes place only because of the activation, resulting from the activation of the Ras or Ras-like signal pathway, of a specific transcription factor, at a particular time or the expression rate of this reporter gene based on the transcription or translation product under said conditions, and in step (c) the measurement of the concentration of the ligand in the sample takes place by comparing the measured values with corresponding values measured for known standard concentrations of the ligand.

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Claim 50 (Previously Presented) An assay as claimed in claim 48, characterized in that in step (a) cells in which the inactive or inactivatable Ras or Ras-like signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for cell reproduction are employed, and the quantitative detection of the extent of the activation of the Ras or Ras-like signal pathway in step (b) takes place indirectly by determining the reproduction of the cells at a fixed time or the reproduction rate of the cells under said conditions, and in step (c) the measurement of the concentration of the ligand in the sample takes place by comparing the measured values with corresponding values measured for known standard concentrations of the ligand.

Claim 51 (Previously Presented) An *in vivo* assay for determining whether a compound is able to alter a binding activity of a ligand-binding section of a receptor in relation to a ligand, characterized by the following steps:

(a) contacting the ligand in the presence of the compound with cells as claimed in any of claim 30 under conditions with which in the absence of the membrane receptor the Ras or Ras-like signal pathway in the cells cannot be activated, where the membrane receptor contains said ligand-binding section, and the effector protein or polypeptide whose binding to a membrane component depends on the binding of or, alternatively, the lack of binding of a ligand to the ligand-binding section of the membrane receptor, as defined in claim 30, is able to activate this Ras or Ras-like signal pathway,

(b) investigating whether and, where appropriate, to what extent activation of the Ras or Ras-like signal pathway takes place,

(c) comparing the result of the investigation in step (b) with a result of an investigation obtained when the assay is carried out in the absence of the compound.

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Claim 52 (Previously Presented) An assay as claimed in claim 51, characterized in that step (b) comprises detecting the activation of the Ras or Ras-like signal pathway via reporter gene expression which takes place where appropriate and only because of the activation, resulting from the activation of the Ras or Ras-like signal pathway, of a specific transcription factor, and the quantitative detection, which takes place where appropriate, of the extent of the activation of the Ras or Ras-like signal pathway comprises determining the amount, present in the cells, of transcription or translation product of the reporter gene at a particular time or the expression rate of this reporter gene based on the transcription or translation product under said conditions, and in the case where the comparison in step (c) reveals that stronger expression of the reporter gene occurs in the presence of the compound, an agonistic effect of the compound is indicated, and in the case where the comparison in (c) reveals that lower expression of the reporter gene occurs in the presence of the compound, an antagonistic effect of the compound is indicated.

Claim 53 (Previously Presented) An assay as claimed in claim 52, characterized in that it is carried out under conditions with which no reproduction of the cells occurs.

Claim 54 (Previously Presented) An assay as claimed in claim 51, where in step (a) there is use of cells in which the inactive Ras or Raslike signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for cell reproduction, and step (b) comprises investigating whether and, where appropriate to what extent, the cells are able to reproduce under said conditions, and in the case where the comparison in step (c) reveals that greater cell reproduction occurs in the presence of the compound, an agonistic effect of the compound is indicated, and in the case where the comparison in step (c) reveals that less cell reproduction occurs in the presence of the compound, an antagonistic effect of the compound is indicated.

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Claim 55 (Previously Presented) An *in vivo* assay for detecting whether a polypeptide or protein has a ligand-binding function of a receptor, characterized by the following steps:

(a) contacting cells as claimed in claim 30 with the ligand under conditions with which in the absence of the membrane receptor, defined in claim 30, a Ras or Ras-like signal pathway in the cells cannot be activated, where the ligand-binding section of the membrane receptor comprises the polypeptide or protein to be investigated or consists thereof, and where the effector protein or polypeptide whose binding to a membrane component depends on the lack of binding of a ligand to the ligand-binding section of the membrane receptor, is able to activate the inactive Ras or Ras-like signal pathway,

(b) investigating whether an activation of the Ras or Ras-like signal pathway has taken place, where detection of the activation of the Ras or Ras-like signal pathway indicates that the ligand-binding section of the membrane receptor and, accordingly, the polypeptide or protein to be investigated has a ligand-binding function of a receptor.

Claim 56 (Previously Presented) An assay method as claimed in claim 55, characterized in that the ligand-binding section of the membrane receptor present in the cells is derived from a naturally occurring receptor section by mutation.

Claim 57 (Previously Presented) An assay as claimed in claim 55, where step (b) comprises detecting the activation of the Ras or Ras-like signal pathway via reporter gene expression which takes place where appropriate and only because of the activation, resulting from the activation of the Ras or Ras-like signal pathway, of a specific transcription factor, where detection of the expression of the reporter gene indicates the ligand-binding function of the ligand-binding section of the membrane receptor and, accordingly, of the polypeptide or protein to be investigated.

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Claim 58 (Previously Presented) An assay as claimed in claim 55, where in step (a) cells in which the inactive or inactivatable Ras or Ras-like signal pathway is a signal pathway which acts on the cell cycle and whose activation is essential for cell reproduction are employed, and step (b) comprises investigating whether the cells are capable of reproduction under said conditions, where detection of the ability of the cells to reproduce indicates the ligand-binding function of the ligand-binding section of the membrane receptor and, accordingly, of the polypeptide or protein to be investigated.

Claim 59 (Currently Amended) An *in vivo* assay for determining whether a polypeptide or protein has ligand-binding function of a receptor, characterized by the following steps:

(a) contacting the cells as claimed in claim 30 with the ligand under conditions with which in the absence of the membrane receptor, as defined in claim 30, a Ras or Ras-like signal pathway in the cells cannot be activated, where the ligand-binding section of the membrane receptor comprises the polypeptide or protein to be investigated or consists thereof, and where the effector protein or polypeptide whose binding to a membrane component depends on the lack of binding of a ligand to the ligand-binding section of the membrane receptor, is able to activate the inactive Ras or Ras-like signal pathway,

(b) investigating whether an activation of the Ras or Ras-like signal pathway has taken place,

(c) investigating cells as employed in step (a) under conditions with which the Ras or Ras-like signal pathway in the cell cannot be activated in the absence of the membrane receptor, for activation of the Ras or Ras-like signal pathway in the absence of ligands, where a detection of the activation of the Ras or Ras-like signal pathway in the absence of the ligand and the inactivity of the Ras or Ras-like signal pathway in the presence of the ligand indicates that the ligand-binding section of the membrane receptor and, accordingly, the polypeptide or protein to be investigated has a ligand-binding function of a receptor.

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Claim 60 (Previously Presented) A kit for use in an assay as claimed in claim 35, which comprises cells as claimed in claim 35.

Claim 61 (Previously Presented) A kit for use in an assay as claimed in claim 35, which comprises components (a) and (b) indicated below and, where appropriate, additionally one or both of components (c) and (d) indicated below:

(a) cells in which at least under certain conditions a Ras or Ras-like signal pathway cannot be activated;

(b) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes a membrane receptor, as defined in claim 35, where the effector protein or polypeptide whose binding to a membrane component depends on the binding or, alternatively, lack of binding of ligand to the ligand-binding section of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway in the cells mentioned under (a);

(c) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes the effector protein or polypeptide which, in the event of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section of the membrane receptor, is able to bind to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and which is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding possible to the component of the membrane, where appropriate via other proteins or polypeptides (adaptors);

(d) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes at least one adaptor protein, via which the effector protein or polypeptide is able, when there is binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor, to bind to a component of the membrane.

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Claim 62 (Previously Presented) A kit for use in an assay as claimed in claim 35, which comprises components (a) and (b) indicated below and, where appropriate, additionally one or both of components (c) and (d) indicated below:

- (a) cells in which a Ras or Ras-like signal pathway cannot be activated at least under certain conditions;
- (b) a nucleic acid vector which comprises, in suitable arrangement;
 - a DNA section which encodes a membrane-localization signal of a membrane receptor, as defined in claim 35;
 - a DNA section which encodes a mediator section of a membrane receptor, as defined in claim 35; and
 - a suitably arranged insertion site for functional insertion of a DNA sequence which encodes a ligand-binding section, as defined in claim 35, where, after insertion of a DNA sequence for the ligand-binding section, the nucleic acid vector comprises a complete expressible gene for a membrane receptor, as defined in claim 35, where the effector protein or polypeptide whose binding to a membrane component depends on the binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway in the cells mentioned under (a);
- (c) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes the effector protein or polypeptide which, in the event of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section of the membrane receptor, is able to bind to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and which is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding possible to the component of the membrane, where appropriate via other proteins or polypeptides (adaptors);
- (d) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes at least one adaptor protein, via which the effector protein or polypeptide is able, when

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there is binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor, to bind to a component of the membrane.

Claim 63 (Previously Presented) A kit for use in an assay as claimed in claim 55, which comprises cells as claimed in claim 55, where the membrane receptor, as defined in claim 55, present therein comprises a ligand-binding section comprising or consisting of a polypeptide or protein suspected of having a ligand-binding function of a receptor.

Claim 64 (Previously Presented) A kit for use in an assay as claimed in claim 55, which comprises components (a) and (b) indicated below and, where appropriate, additionally one or both of components (c) and (d) indicated below:

(a) cells in which a Ras or Ras-like signal pathway cannot be activated at least under certain conditions;

(b) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes a membrane receptor, as defined in claim 55, where the ligand-binding section of the membrane receptor comprises a polypeptide or protein suspected of having a ligand-binding function of a receptor, or is formed therefrom, and the effector protein or polypeptide whose binding to a membrane component depends on the binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway in the cells mentioned under (a);

(c) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes the effector protein or polypeptide which, in the event of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section of the membrane receptor, is able to bind to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and which is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding possible to the component of the

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membrane, where appropriate via other proteins or polypeptides (adaptors);

(d) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes at least one adaptor protein, via which the effector protein or polypeptide is able, when there is binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor, to bind to a component of the membrane.

Claim 65 (Previously Presented) A kit for use in an assay as claimed in claim 55, which comprises components (a) and (b) indicated below and, where appropriate, additionally one or both of components (c) and (d) indicated below:

(a) cells in which a Ras or Ras-like signal pathway cannot be activated at least under certain conditions;

(b) a nucleic acid vector which comprises, in suitable arrangement;

- a DNA section which encodes a membrane-localization signal of a membrane receptor, as defined in claim 55;

- a DNA section which encodes a mediator section of a membrane receptor, as defined in claim 55; and

- a suitably arranged insertion site for functional insertion of a DNA sequence which encodes a polypeptide or protein suspected of having a ligand-binding function of a receptor, where, after insertion of a DNA sequence for the ligand-binding section, the nucleic acid vector comprises a complete expressible gene for a membrane receptor, where the effector protein or polypeptide whose binding to a membrane component depends on the binding or, alternatively, lack of binding of a ligand to the ligand-binding section, formed from the polypeptide or protein suspected of having a ligand-binding function of a receptor, of the membrane receptor is able to activate the inactive Ras or Ras-like signal pathway in the cells mentioned under (a);

(c) a nucleic acid vector into which is expressibly inserted a DNA sequence which

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encodes the effector protein or polypeptide which, in the event of ligand binding or, alternatively, lack of ligand binding to the ligand-binding section of the membrane receptor, is able to bind to a component of the membrane, where appropriate via other proteins or polypeptides (adaptors), and which is in the form of a fusion protein of an effector section with an adaptor protein or polypeptide which makes binding possible to the component of the membrane, where appropriate via other proteins or polypeptides (adaptors);

(d) a nucleic acid vector into which is expressibly inserted a DNA sequence which encodes at least one adaptor protein, via which the effector protein or polypeptide is able, when there is binding or, alternatively, lack of binding of a ligand to the ligand-binding section of the membrane receptor, to bind to a component of the membrane.

Claim 66 (Previously Presented) A kit as claimed in claim 60, in which the cells additionally contain a construct comprising a binding site for a transcription factor whose activation results from an activation of a specific Ras or Ras-like signal pathway whose activation is to be detected by the assay, a minimal promoter and a reporter gene functionally linked thereto, where the minimal promoter is activated as a result of binding of the activated transcription factor to its binding site.

Claim 67 (Previously Presented) A kit as claimed in claim 60, characterized in that it additionally contains a transformation or transfection vector with a construct comprising a binding site for a transcription factor whose activation results from an activation of a specific Ras or Ras-like signal pathway whose activation is to be detected by the assay, a minimal promoter and a reporter gene functionally linked thereto, where the minimal promoter is activated transcription factor to its binding site.

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Claim 68 (Previously Presented) A kit as claimed in claim 60, characterized in that it additionally contains a transformation or transfection vector with a construct comprising a binding site for a transcription factor comprising a binding site for a transcription factor whose activation results from an activation of a specific Ras or Ras-like signal pathway whose activation is to be detected by the assay, a minimal promoter and an insertion site, suitably arranged for expression controlled by the minimal promoter, for insertion of a reporter gene, where the minimal promoter is activated as a result of a binding of the activated transcription factor to its binding site.

Claim 69 (Previously Presented) A kit as claimed in claim 60, which contains the cells immobilized or enclosed in microchambers of a solid carrier, in particular on biochips.

Claim 70 (Previously Presented) A method for identifying polypeptides or proteins, in particular receptors, which have a ligand-binding function of a receptor, which comprises:

- preparing a cell as claimed in claim 1 with a membrane receptor having the features described in claim 1 and comprising the whole of such a polypeptide or protein or a part of such a polypeptide or protein which presumably contains the sequence sections essential for the ligand-binding function, and

- using this cell to carry out an *in vivo* assay method for detecting whether a polypeptide or protein has a ligand-binding function of a receptor, as claimed in claim 1.

Claim 71 (Previously Presented) A cell as claimed in claim 1, wherein the adaptor comprises Grb2 polypeptide.

Claim 72 (Previously Presented) A cell as claimed in claim 1, wherein the adaptor comprises murine Grb2 polypeptide.

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Claim 73 (Previously Presented) A cell as claimed in claim 1, wherein the adaptor comprises Shc polypeptide.

Claim 74 (Previously Presented) A cell as claimed in claim 1, wherein the cell is a eukaryotic cell.

Claim 75 (Previously Presented) A cell as claimed in claim 1, wherein the cell is a prokaryotic cell.

Claim 76 (Previously Presented) A cell as claimed in claim 1, wherein the cell is a yeast cell lacking cell walls.

Claim 77 (Previously Presented) A cell as claimed in claim 1, wherein the cell is a *Saccharomyces cerevisiae* yeast cell.

Claim 78 (Previously Presented) A cell as claimed in claim 1, wherein the cell is a *Saccharomyces cerevisiae* yeast cell strain cdc25-2.

Claim 79 (Previously Presented) A cell as claimed in claim 1, wherein the membrane receptor is the human epidermal growth factor receptor.

Claim 80 (Currently Amended) A cell as claimed in claim 1, wherein the membrane receptor is coded for by a nucleic acid which has been introduced into said cell.

Claim 81 (Currently Amended) A cell as claimed in claim 1, where the fusion protein is coded for by a nucleic acid which has been introduced into said cell.

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Claim 82 (Previously Presented) A cell as claimed in claim 1, wherein the cell is a yeast cell and the membrane receptor is the human epidermal growth factor receptor and the fusion protein comprises a constitutively active human ras polypeptide fused to a murine Grb2 polypeptide.

Claim 83 (Previously Presented) A cell as claimed in claim 82, wherein the ras protein lacks the CAAX box.

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